ANNEX I.
OUR PATENTABILITY INDEX

There are many elements the protection of which, in legal terms, is desirable (see the orange box below). However, not all of them are susceptible to patent, but a small group (in white) that must also have some characterictics, namely: **Novelty**, **Inventive Step** and **Industrial Application**.

An idea – Scientific Theories – Mathematical Methods – Art Creations – Commercial or Economical Activities – Computer Programs or Software – Objects (Products...)* – Presenting Information Methods – Vegetable or Animal Varieties – Images – Designs – Words or Sentences – Signs – Plays (Artistic, Literary, Scientific) – Procedures or Manufacturing Methods

*If it only provides an improvement to an existing product: Utility Model

Table 1. *Different human creations are shown. In white, see human-made things/discoveries that could be patented. In orange, the ones that in case of being protected would need other kind of legal (non-patent protection).*

Traditionally, experts decide whether something is patentable or not. In an effort to assist those experts, we, the Valencia Biocampus iGEM team, describe below an intuitive formula that might be helpful for them and also for other actors in SynBio (e.g. engineers, scientists, DIY biologists) when it comes time to take a decision. The formula we propose is based in internationally accepted standards and articles related to the topic (see bibliography and references).

A. THE FORMULA. F_0

Extended F_0 ecuation

$$\text{Patentability Index } [\mathbf{P.I.}] = \text{ Morality } (\mathbf{M}) \text{ x Novelty } [\mathbf{N}] \text{ x (Inventive Step } [\mathbf{A}])^{\log\left(\frac{\text{Inventive Step [A]+ Industrial application [I]}}{2}\right)}$$

Please note that we introduce in the formula a non-legal term, morality.[1]

Abreviatted F_0 ecuation

$$\mathbf{P.I.} = \mathbf{M} \text{ x } \mathbf{N} \text{ x } (\boldsymbol{A})^{\log\left(\frac{\mathbf{A}+\mathbf{I}}{2}\right)}$$

[1] In Europe, the terms of morality & ordre public are mentioned in European patent Convention.

The numerical limits of the formula and the mathematical interpretation (modelling) of the P.I. value are shown at the end of Annex IA.

How does the formula work?

By answering specific question the values of the different parameters in the equation can be introduced.

Previous questions (If any of the answers is "Yes" the invention could not be patented):

- Is your invention about or related to the following fields…

- scientific theories and mathematical methods?	Yes	No
- artistic/literary creations?	Yes	No
- aesthetic creations?	Yes	No
- schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers?	Yes	No
- methods for presenting information.	Yes	No

Breakdown of terms

- **Morality (M). Values: 0/1**

The value of **M** is not arbitrary, but a result of a questionnaire. If any of the answers is "Yes", the term of morality (**M**) automatically becomes zero.

- This invention relates to…

- isolated genes?*	Yes	No
- sequenced DNA?*	Yes	No
- medical procedures?	Yes	No
- embryonic stem cells?	Yes	No
- methods of chromosome transfer?	Yes	No
- mixing of human and animal species?	Yes	No

- Could this invention result in…

- denigration or human dignity?**	Yes	No
- destruction of human life?	Yes	No
- ownership of human life?	Yes	No
- spread of pollution or disease?	Yes	No
- loss of genetic diversity?	Yes	No

If the aim is to protect the DNA* per se*, it must be noted that patent eligible subject matter is "anything under the sun made by humans". The relevant point here is not if the creation is a living or an inanimate thing, but if they are* ***products of nature**, whether living or nor, or* ***human made inventions****.*

To sum up: *DNA per se. Not patentable.* ✖

Applications arose from the presence/use of that sequence. Patentable. ✔

*** Given the high diversity of the use of dignity throughout the judicial world, human dignity could be understood as a set of three minimum elements: an ontological, a relational and a limited-state claims. The ontological one refers to "the inherent dignity of man"; the relational claim relates to the intrinsic worth and the recognition respect of it by others; finally the third claim recognizes the intrinsic worth of individual in such a way that the state should exist for the sake of the individual human being, and not* viceversa.

- **Novelty (**N**). Values: 0/1.**

Similarly, **N** is calculated from the answers to several questions. If any of the answers is "Yes", the term of novelty automatically becomes zero.

Is there a process or product identical to yours (prior state of art)?*	Yes	No
Has the invention been used in public so its operation made is known?	Yes	No
Have the details of the invention publicly disseminated?**	Yes	No

**For answering this question, one has to perform an online search, using the invention/creation keywords, in the following browsers/databases:*

European Patent Office (EPO) *Spanish Patent & Trademark Office (OEPM)*

United States Patent and Trademark Office (USPTO) *Japan Patent Office (JPO)*

PubMed Database *SCOPUS Database*

An invention shall be taken to be new if it does not form part of the state of the art.

The state of the art in the case of an invention shall be taken to comprise all matter (whether a product, a process, information about either, or anything else) which has at any time before the priority date of that invention been made available to the

public (whether in the country where the invention would be patented or elsewhere) by written or oral description, by use or in any other way.

***The discussion of the details related to the invention with fellow researchers, partners and advisors is considered as confidential. It is highly recommended to sign confidential agreements.*

- **Inventive Step (A). Values: 1-10.**

By contrast with **M** and **N**, inventive step (**A**) may be any value between 1 and 10. This test has an initial value of 1 and 3 points for each of the options/answers bold marked can be added up a total **A** value of 10.

If the invention/creation is the combination of several ones, are their properties or functionality predictable if you know all its components? *	Yes	**No**
If the invention/process is the solution to a problem, are there different solutions possible so the inventor had to research and select the best one?**	**Yes**	No
Is the invention the replacement of one of the components of the product/process for a different one with equivalent properties?	Yes	**No**

**If the properties are greater than the sum of its parts, or better than expected, then it can be considered as a non-obvious invention. And then, the answer to the previous question should be "No".*

Summing up: patentability requires that several features are met (including: surprising technical advantages, unexpected technical effects). Mere aggregations (developments in one way street -lack of alternatives) are not patentable.

***If there is only one solution to a problem in a process, object or invention, and it could be deduced by a person skilled in the art, it might be considered obvious.*

- **Industrial Application (I). Values: 1-10**

This test has an initial value of 1, to which are added 3 points for each of the options/answers bold marked.

Is the industrial field totally clear in the invention description?*	**Yes**	No
Is the main application of the invention related to the private and personal sphere of human being?	Yes	**No**
Is the invention described clear and complete enough for being carried out by a person skilled in		

	the art?**	**Yes**	No
✚	Is the invention a method for treatment of the human or animal by surgery or therapy or a diagnostic method practiced on the human or animal body?***	Yes	**No**

**It must be specified the industry the invention is addressed to (the term "Industry" is far-reading). It is especially important when the invention refers to DNA sequences.*

An invention shall be taken to be capable of industrial application if it can be made or used in any kind of industry, including agriculture.

***Requirement of sufficiency of disclosure.*

Disclosure*: the matter relied upon as prior art must disclose subject matter that, if performed, would necessarily result in an infringement of the patent.*

*******Eliminatory question****. If the answer to this question is "Yes" the P.I. automatically becomes "0". This restriction does not apply to an invention consisting of a substance or composition for use in any such method.*

Limits and mathematical interpretation (modelling of F_0)

As we mentioned above, our HP team has developed an equation for the field of intellectual property, based in the current laws on this issue.

$$P = M \cdot N \cdot \left(\frac{A+I}{2}\right)^{\log(A)} \quad (1)$$

Where:

$P \in \{0,1,\dots,9,10\}$ is patentability.

$M \in \{0,1\}$ is morality.

$N \in \{0,1\}$ is novelty.

$A \in \{1,2,\dots,9,10\}$ is inventive step.

$I \in \{1,2,\dots,9,10\}$ is industrial application.

Both morality and novelty are strict criteria with only two possible values: they must be one in order to be patentable and they are the main barriers in patentability. Once they are overcome, patentability becomes more ¿subjective? This term is the most interesting, in a mathematical way, to analyse. So we can define:

$$P_c = \left(\frac{A+I}{2}\right)^{\log(A)} \quad (2.a)$$

or

$$P_c = A^{\log\left(\frac{A+I}{2}\right)} \quad (2.b)$$

Proof:

$$P_c = \left(\frac{A+I}{2}\right)^{\log(A)} \rightarrow \log(P_c) = \log\left(\left(\frac{A+I}{2}\right)^{log(A)}\right) \rightarrow \log(P_c) = log(A) \cdot log\left(\frac{A+I}{2}\right) \rightarrow$$

$$\rightarrow \log(P_c) = \log\left(A^{log\left(\frac{A+I}{2}\right)}\right) \rightarrow P_c = A^{\log\left(\frac{A+I}{2}\right)}$$

Using 2.b equation, A variable is more important than I. Independently of any value of I, patentability is always one when A takes the value of one.

The other extreme situation takes places when A is maximal: The patentability increases linearly with the Industrial application.

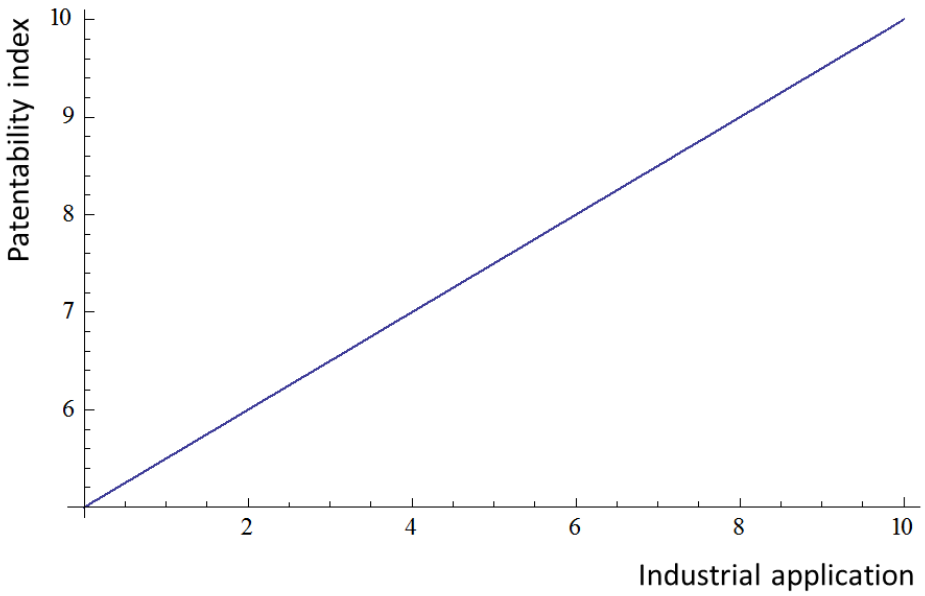

Figure 3. At a maximal value of **A**, the Patentability Index (**P.I.**) value increases in a linear way as industrial application as the Industrial application (**I**) does.

Figure 4 shows three plots depicting the patentability as function of the **Industrial application** (I) and the **Inventive step** (A) -the terms of **Morality** (M) and **Novelty** (N) must be necessarily one; if not, the final value of the **Patentability Index** (P.I.) would be zero and there would be no need to A and I values.

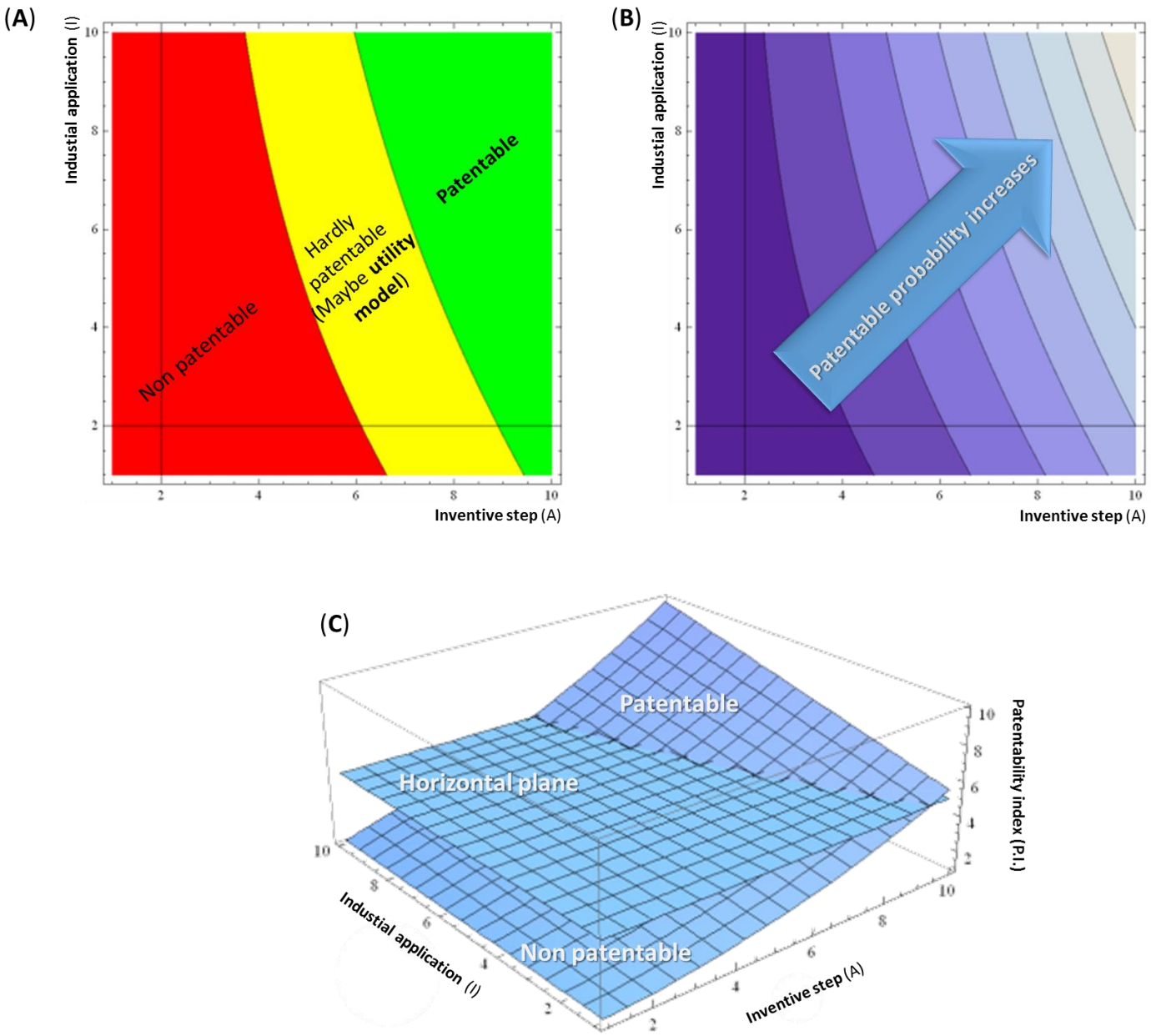

Figure 4. A, main regions of patentability: no patentability in red, hardly patentable in yellow (in this case the inventor should consider protecting by utility model when allowed in the particular country or improving the invention in order to rise it to a stronger position in terms of patentability), and total patentability in green. **B**, proportional regions depending of the different values taken by the A & I parameters (note that the index final value strongly relies on A rather than on I). And finally, the third plot (**C**) shows the graphical representation of the formula in three dimensions with the separation at threshold of 5. The horizontal plane sets the limit of patentability.

B. DIRECTED EVOLUTION OF THE FORMULA (Experts' comments and suggestions)

In this subpart of the **Annex I,** the comments and suggestions from the experts we sent the draft of the report to, are shown. We wanted this process to be like an article review in which we considered those comments as minor/major revisions to build our definitive version of the formula.

Experts' comments and suggestions

Expert1:

"Should the formula (and its criteria / questions) be applicable internationally, i.e. beyond Europe? (e.g. regarding Morality (M) in the formula: US patent law does not (explicitly) require that inventions meet "moral standards", while the 'European Directive on Legal Protection of Biotechnological Inventions' does (and prohibits inventions that offend the "order public" / public morality)."

"Some sentences/explanations on what resources the user of the formula should refer to in order to answer human dignity questions (presumably you refer to case law or present/past judgments on similar/related patent claims; in any case, the approach might specified) could be included."

"Decisions to file a patent claim are dependent on many interests/conditions and two different persons can take opposite decisions on the basis of the same information. This contextual interpretation might be stressed at some point (and it seems in line with your view that the formula does not replace "human decisions")."

Expert2:

"It would be appropriate to mention the TRIPS Agreement and the European Directive 98/44 on the legal protection of biotechnological inventions."

"The legal rules make reference to "ordre public and morality". The legal concepts are not exactly the same. If you want to summarize this concept with the expression "morality" it would be appropriate to specify and explain this."

"The analysis of the cases Diamond v. Chakrabarty, Association forMolecular Pathology et al. v. Myriad Genetics, (US cases) and Monsanto Technology LLC contra Cefetra BV e altri (C-428/08) (UE Court of Justice) would be highly recommended." (Related to the morality test)

"In Association for Molecular Pathology et al. v. Myriad Genetics you will find that not necessarily a genetic sequence used for industrial reasons shall be patented [...], the difficulty in these kind of situation is not necessarily based on morality, but on the inventive step."

Expert3:

“Is morality really a completely "non-legal term"?”

Expert4:

“In your notes it might be worth pointing out that non-natural (synthetic) DNA sequences are patentable.”

“Even if something can be patented (even if it fulfils both the moral and the technical criteria for patentability), then there may still be reasons that someone might decide not to go ahead and patent. One reason might be to avoid ‘patent thickets’ or ‘blocking patents’, where there are so many patents that this inhibits the progress of research. Heller and Eisenberg’s paper, is a classic reference here. I think one of the motivations behind openness in synthetic biology is related to this. It is to attempt to stop people patenting the parts, which would make it very hard to claim IP on a device or system that used a combination of many different parts.”

“After you have had the final results of your survey, it would be interesting if you could reflect on these results, and discuss what they mean for your formula.”

Expert5:

“How exactly RRI fits in the discussion and formula you present in the rest of the report, including Annex II? In the formula you faithfully try to represent the internationally accepted standards relating to IPR. RRI could also be used in this context as a framework which extends the set of internationally accepted standards to include broader societal and ethical considerations in deciding whether you would like to patent a particular achievement. So, instead of the M (morality) you could include an R (responsibility) in your formula, whereby I would prefer to scale the value of R from 0 to 10.”

Annex IC *describes the improved version of the equation we have prepared according to the experts’ comments and suggestions. The main improvements are: the change of the* ***M*** *(morality, possible values: 0/1) term of the initial formula for* ***R*** *(responsibility, possible values: 0-1) and the addition of jurisprudence and articles for clarifying the questions of each formula section.*

C. THE FINAL FORMULA. F_1

Extended F_1 ecuation

$$\text{Patentability Index } [\mathbf{P.I.}] = \text{ Responsibility}(\mathbf{R}) \text{ x Novelty } [\mathbf{N}] \text{ x (Inventive Step } [\mathbf{A}])^{\log\left(\frac{\text{Inventive Step [A]+ Industrial application [I]}}{2}\right)}$$

Please note that we introduce in the formula a non-legal term, responsibility.

Abreviatted F_1 ecuation

$$\mathbf{P.I.} = \mathbf{R} \text{ x } \mathbf{N} \text{ x } (\boldsymbol{A})^{\log\left(\frac{\mathbf{A}+\mathbf{I}}{2}\right)}$$

The numerical limits of the formula and the mathematical interpretation (modelling) of the P.I. value are shown at the end of Annex IA.

How does the formula work?

By answering specific question the values of the different parameters in the equation can be introduced.

Previous questions (If any of the answers is "Yes" the invention could not be patented):

- Is your invention about or related to the following fields...

- scientific theories and mathematical methods?	Yes	No
- artistic/literary creations?	Yes	No
- aesthetic creations?	Yes	No
- schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers?	Yes	No
- methods for presenting information.	Yes	No

Breakdown of terms

- **Responsibility (R). Values: 0-1**

The value of **R** is not arbitrary, but a result of a questionnaire.

If any of the answers for the following questions is "Yes", the term of responsibility (**R**) automatically becomes **zero**.

- This invention relates to...

- isolated genes?*	Yes	No
- sequenced DNA?*	Yes	No
- medical procedures?	Yes	No
- embryonic stem cells?	Yes	No
- methods of chromosome transfer?	Yes	No
- mixing of human and animal species?	Yes	No

- Could this invention result in...

- denigration or human dignity?**	Yes	No
- destruction of human life?	Yes	No
- ownership of human life?	Yes	No
- spread of pollution or disease?	Yes	No
- loss of genetic diversity?	Yes	No

If the aim is to protect the DNA* per se*, it must be noted that patent eligible subject matter is "anything under the sun made by humans". The relevant point here is not if the creation is a living or an inanimate thing, but if they are **products of nature, whether living or nor, or **human made inventions**.*

To sum up: *DNA per se. Not patentable.* ✖

Applications arose from the presence/use of that sequence. Patentable. ✔

*IMPORTANT: **Non-natural** (synthetic) **DNA** sequences **are** patentable ("human made")*

For clarifying this question:

Association for Molecular Pathology et al. v. Myriad Genetics (USA): "merely isolating genes that are found in nature does not make them patentable, but cDNA is patent eligible because it is not naturally occurring".

***Given the high diversity of the use of dignity throughout the judicial world, human dignity could be understood as a set of three minimum elements: an ontological, a relational and a limited-state claims. The ontological one refers to "the inherent dignity of man"; the relational claim relates to the intrinsic worth and the recognition respect of it by others; finally the third claim recognizes the intrinsic worth of individual in such a way that the state should exist for the sake of the individual human being, and not* viceversa.

If any of the answers for the following questions is bold marked **0.3 points** can be added up to a total **R** value of 1.

For clarifying the questions of this part of the questionnaire, it is advisable to read the following article/case:
Heller, M.A. & Eisenberg R.S. Can patents deter innovation? The anticommons in biomedical research. Science (1998) 280 (698), 698-701

May the fact that the invention is protected result in a blockage of the research progress? *	Yes	**No**
Would the patent release some information or advanced useful -in terms of technology or research-, that in case of not being patented would be hidden (by trade secret, for example)?	**Yes**	No
Could the invention result in a solution to an important societal problem?**	Yes	**No**

**If the answer is affirmative, one might decide not to go ahead on patenting considering the possible damage to the growth of knowledge and to the scientific development, even when the moral and the technical criteria for patentability result in a positive Patentability Index value.*

*** If the answer is affirmative, one might decide not to go ahead on patenting considering the welfare that would be restricted to the population, even when the moral and the technical criteria for patentability result in a positive Patentability Index value.*

- **Novelty (**N**). Values: 0/1.**

Similarly, **N** is calculated from the answers to several questions. If any of the answers is "Yes", the term of novelty automatically becomes zero.

For clarifying the questions of this part of the questionnaire, it is advisable to read the following article/case:
Merrell Dow Pharmaceuticals v H N Norton & Co [1996] RPC 76

Is there a process or product identical to yours (prior state of art)?*	Yes	No
Has the invention been used in public so its operation made is known?	Yes	No
Have the details of the invention publicly disseminated?**	Yes	No

**For answering this question, one has to perform an online search, using the invention/creation keywords, in the following browsers/databases:*

European Patent Office (EPO) *Spanish Patent & Trademark Office (OEPM)*

United States Patent and Trademark Office (USPTO) *Japan Patent Office (JPO)*

PubMed Database *SCOPUS Database*

An invention shall be taken to be new if it does not form part of the state of the art.

The state of the art in the case of an invention shall be taken to comprise all matter (whether a product, a process, information about either, or anything else) which has at any time before the priority date of that invention been made available to the public (whether in the country where the invention would be patented or elsewhere) by written or oral description, by use or in any other way.

***The discussion of the details related to the invention with fellow researchers, partners and advisors is considered as confidential. It is highly recommended to sign confidential agreements.*

- **Inventive Step, Non-Obvious (A). Values: 1-10.**

The inventive step (**A**) may be any value between 1 and 10. This test has an initial value of 1 and 3 points for each of the options/answers bold marked can be added up a total **A** value of 10.

For clarifying the questions of this part of the questionnaire, it is advisable to read the following article/case:
Genentech Inc.'s Patent, [1989] R.P.C. 147 (C.A.)
Biogen Inc. v. Medeva Plc [1997] R.P.C. 1

If the invention/creation is the combination of several ones, are their properties or functionality predictable if you know all its components? *	Yes	**No**
If the invention/process is the solution to a problem, are there different solutions possible so the inventor had to research and select the best one?**	**Yes**	No
Is the invention the replacement of one of the components of the product/process for a different one with equivalent properties?	Yes	**No**

**If the properties are greater than the sum of its parts, or better than expected, then it can be considered as a non-obvious invention. And then, the answer to the previous question should be "No".*

Summing up: patentability requires that several features are met (including: surprising technical advantages, unexpected technical effects). Mere aggregations (developments in one way street -lack of alternatives) are not patentable.

***If there is only one solution to a problem in a process, object or invention, and it could be deduced by a person skilled in the art, it might be considered obvious.*

- **Industrial Application, Capable of Industrial Application, Useful (I). Values: 1-10**

This test has an initial value of 1, to which are added 3 points for each of the options/answers bold marked.

For clarifying the questions of this part of the questionnaire, it is advisable to read the following article/case:
Eli Lilly v Human Genome Sciences [2010] EWCA Civ 33, overruled [2011] UKSC 51

Is the industrial field totally clear in the invention description?*	**Yes**	No
Is the main application of the invention related to the private and personal sphere of human being?	Yes	**No**
Is the invention described clear and complete enough for being carried out by a person skilled in the art?**	**Yes**	No
Is the invention a method for treatment of the human or animal by surgery or therapy or a diagnostic method practiced on the human or animal body?***	Yes	**No**

**It must be specified the industry the invention is addressed to (the term "Industry" is far-reading). It is especially important when the invention refers to DNA sequences.*

An invention shall be taken to be capable of industrial application if it can be made or used in any kind of industry, including agriculture.

***Requirement of sufficiency of disclosure.*

Disclosure*: the matter relied upon as prior art must disclose subject matter that, if performed, would necessarily result in an infringement of the patent.*

*******Eliminatory question****. If the answer to this question is "Yes" the P.I. automatically becomes "0". This restriction does not apply to an invention consisting of a substance or composition for use in any such method.*

D. iGEM VALENCIA BIOCAMPUS SURVEY ON IP

We conducted a survey in order to find out what is the opinion of the society on our patentability formula and our idea of improving the IP framework. Thus, we carried out an online survey – in English and Spanish- focusing on specific groups. These groups are iGEM participants, lawyers, biotechnologists, general public and engineers.

The survey consisted of just a simple question about whether patentability of a technical invention should be decided by the person skilled in the art or it would be better to use a formula. We proposed three options to choose among them:

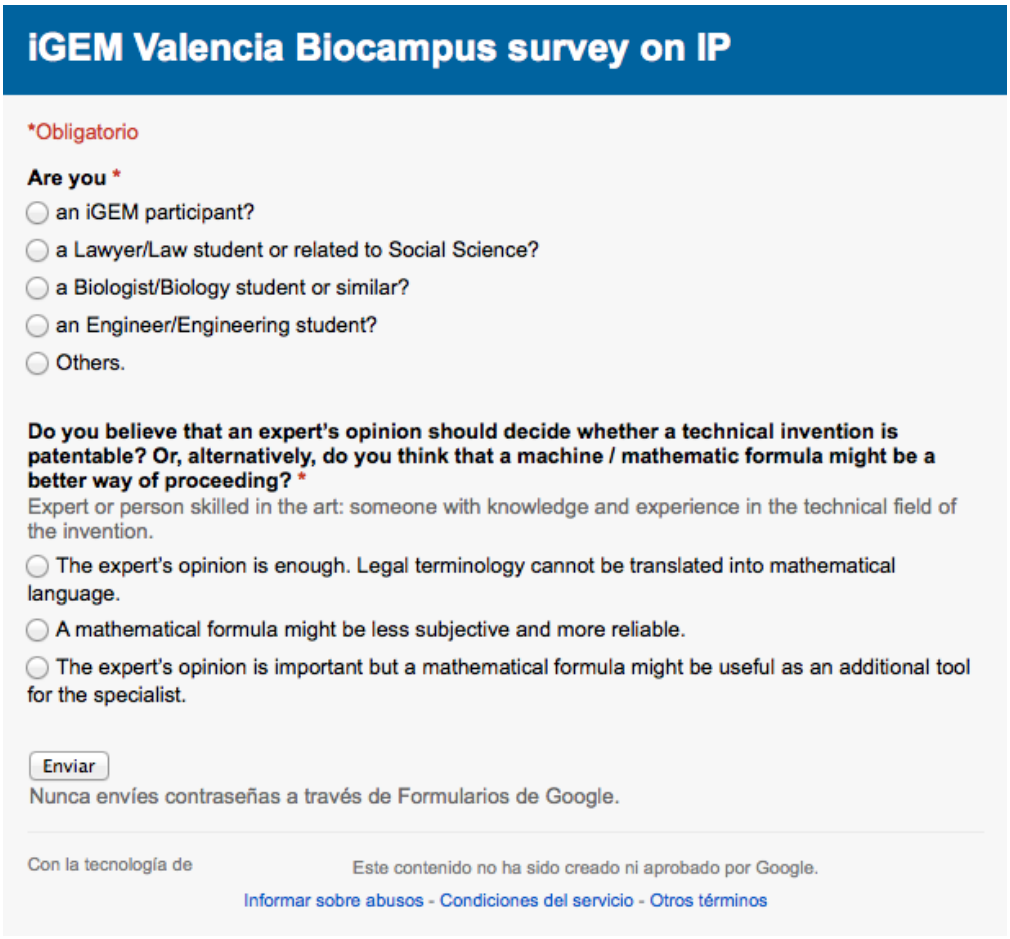

Figure 4. English version of our online survey.

Results of the survey

After two and a half months of the survey start, the results are summarized on the pie charts shown below. The final number of participants was 526. Each group was well-represented (14-26%) and although slight differences among groups are detectable (lawyers were less prone to use maths) a vast majority of respondents (70-83%) found using maths in IP a helpful possibility.

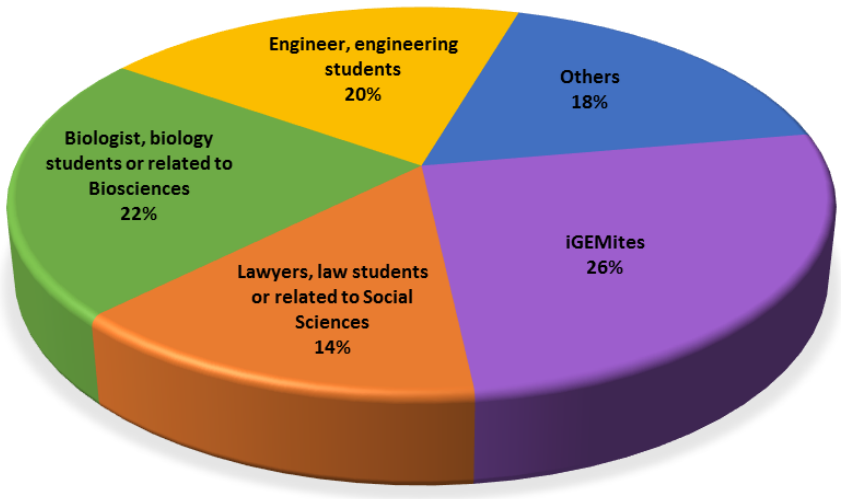

Figure 5. Percentage of participation –by background- in the survey. iGEMites are the majoritarian group with a 26% of participation, in a second place (22%) are the biologists -or related to the field- followed by the engineers or similar (20%). The lowest participation rate is for the lawyers or related to social sciences (only 14% of the responses came from this group).

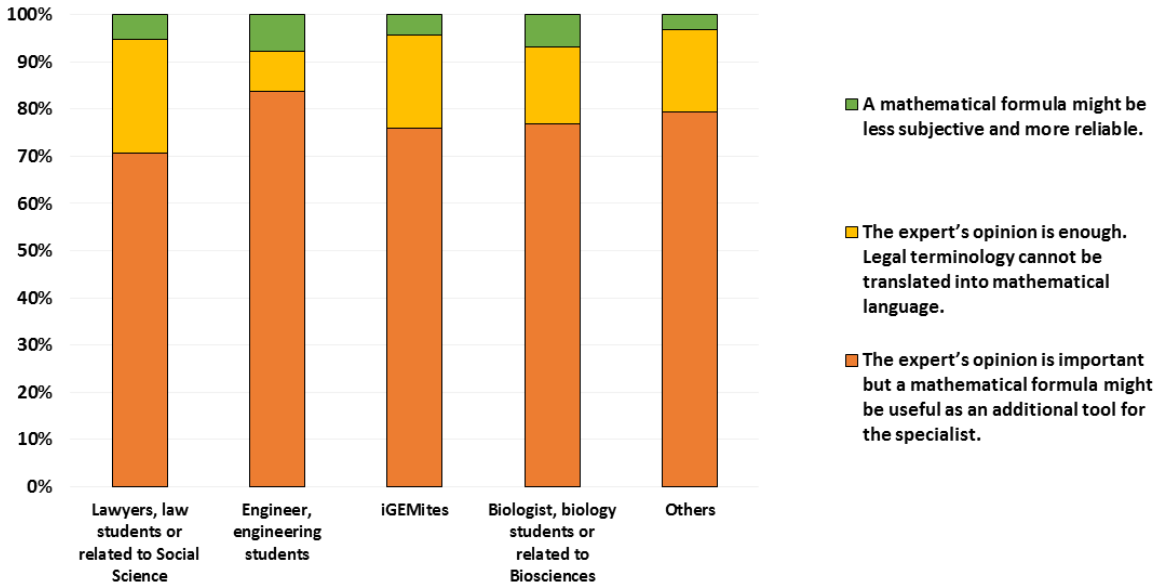

Figure 6. Results of our survey shown in percentage and grouped by field of knowledge. As it can be observed, the favourite option in all the groups was the third one: *The expert's opinion is important but a mathematical formula might be useful as an additional tool for the specialists*. However, differences among the different backgrounds exist being specially pronounced between the group of engineers and lawyers.

E. ANNEX I BIBLIOGRAPHY AND REFERENCES

Article 52. European Patent Convention (EPC).

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Heller, M.A. & Eisenberg R.S. Can patents deter innovation? The anticommons in biomedical research. Science (1998) **280** (698), 698-701

Section 5.Patents. Part II TRIPS Agreements.

Chapter I and II. Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions.

Association for Molecular Pathology et al. v. Myriad Genetics (USA).